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Warren Grant Magnuson Clinical Center

INTRODUCTION

As the research hospital for the National Institutes of Health (NIH), the Warren Grant Magnuson Clinical Center supports clinical investigations conducted by the Institutes. The Clinical Center was specifically designed to bring patient care facilities close to experimental laboratories, to facilitate and expedite the testing and application of basic research findings in the treatment of patients. The 14-story, 290-bed facility employs 600 nurses, 570 allied health professionals, and 1,237 credentialed physicians, dentists, and doctorate-level researchers.

HIGHLIGHTS OF RECENT SCIENTIFIC ADVANCES RESULTING FROM INTERNATIONAL ACTIVITIES

During fiscal year 2000 (FY 00), Clinical Center staff presented research findings at numerous international conferences on subjects such as end-of-life care, ethical research guidelines, surrogate end points, advances in technical magnetic resonance imaging (MRI), the role of the transplant coordinator, transfusion of granulocytes, allogeneic stem cell transplants, management of hepatitis C, and rehabilitation of cancer patients.

Staff also were involved in the formulation and international distribution of investigational medications and in collaborations with international researchers in diverse fields of clinical investigation.

DEPARTMENT OF CLINICAL BIOETHICS

International Research

In a substudy of the Evaluation of Subcutaneous Proleukin in a Randomized International Trial (ESPRIT), on treatment of human immunodeficiency virus (HIV), the Department of Clinical Bioethics is comparing attitudes and experiences regarding ethical issues among (1) institutional review boards and research ethics committees, (2) researchers, and (3) cooperative project assur-

ance contacts. A separate protocol has been submitted for a study on ethical issues in subjects enrolled in ESPRIT.

In June 2000, a staff member traveled to Amsterdam, the Netherlands, to collaborate with Erasmus University on an end-of-life care project.

International Training

The Department continues to collaborate with the John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC), NIH, to develop training programs focused on enhancing bioethics knowledge and skills in developing countries. In concert with the National Institute of Allergy and Infectious Diseases, NIH, the Department is planning a course to train African researchers. In addition, several African investigators from Johns Hopkins University, Baltimore, Maryland, are participating in the Clinical Bioethics 1st-Year Fellows' Seminar, which offers both a history and a broad overview of the field of bioethics.

Other training activities included the following:

- presentation on Ethical Issues in Multinational Vaccine Trials, at the University of Illinois Medical Center, in Chicago, Illinois, on October 15, 1999;

- presentation on International Clinical Research: Responsiveness to the Health Needs of the Community, at a meeting of the American Society for Bioethics and the Humanities, in Philadelphia, Pennsylvania, on October 28, 1999;

- presentation on the ethical challenges in international research, research ethics, and institutional review board responsibilities, at Georgetown University, Washington, D.C., on February 24, 2000;

- presentation on the Quality of Cancer Care, at the meeting of the International Advisory Board on Bioethics on Quality of Health Care and Patients' Rights, in Port of

Spain, Trinidad and Tobago, on February 24, 2000;

- participation in an FIC meeting in Bethesda, Maryland, on March 20–21, 2000, to plan for a global bioethics forum in Bangkok, Thailand, in October 2000, and to consider a draft proposal for revision of the international guidelines for ethical assurance of research;

- meeting of the International Society of Infectious Diseases Training Program, to discuss research ethics, in Bethesda, Maryland, on April 19, 2000;

- meeting of the National Institute of Mental Health (NIH) Work Group on Ethical Issues in Human Studies, in Bethesda, Maryland, on April 28, 2000;

- session of the Panel on Ethical Issues, at the Emerging Infectious Diseases Conference on International Codes and Guidelines: Ongoing Challenges, in Atlanta, Georgia, on July 17, 2000; and

- participation as a member of the international working party, in the development of Operational Guidelines for Ethics Committees That Review Biomedical Research, which was published by the United Nations Development Program, the World Health Organization (WHO), and the World Bank, in 2000.

International Meetings

Department staff participated in various capacities at international meetings during FY 00:

- made a presentation on Euthanasia and Physician Assisted Suicide, at the Academy Colloquium on Epidemiological and Clinical Aspects of End of Life Decision Making, of the Royal Netherlands Academy of Arts and Sciences, in Amsterdam, on October 7–10, 1999;

- participated at the request of WHO in a working meeting about transmission-blocking malaria vaccines, in Bethesda, Maryland, on December 3–4, 1999;

- provided consultation on the revision

of the international ethical guidelines for biomedical research involving human subjects, at a meeting of the Council for the International Organization of Medical Sciences, in Geneva, Switzerland, on March 14–17, 2000;

- served on the International Advisory Board of PAHO/WHO and spoke on Equity in Health: Bioethical Dimensions, in Panama City, Panama, on May 2–3, 2000;

- participated at the Commonwealth Fund/Nuffield Trust Ditchley Conference on Improving Health Care in the United States and the United Kingdom: Strategies for Change and Action, in Oxfordshire, England, on June 9–11, 2000;

- gave a presentation on international perspectives on research with adults unable to consent, at the meeting of the World Psychiatric Association Congress, entitled From Clinical Practice to Research: Rethinking Psychiatry, in Paris, France, on June 27, 2000;

- attended the 4th International Congress on Thanatology and Suicidality, in Stockholm, Sweden, on August 28–30, 2000; and

- made a presentation at the 5th World Congress on Bioethics, Law, and Public Policy, in London, England, on September 20, 2000.

Staff from the Department also organized a symposium on International Health Disparities, to be held in Bethesda, Maryland, in October 2000.

CLINICAL PHARMACOLOGY

International Meetings

On November 30–December 2, 1999, the Senior Advisor in Clinical Pharmacology at the Clinical Center attended the annual meeting of the European Federation for Pharmaceutical Sciences, in Basel, Switzerland. The meeting, which focused on optimizing drug development and streamlining proof of concept, was attended by industrialists, academics, and government employees. The Senior Advisor spoke on the development and evaluation of biomarkers and surrogate end points, chaired a seminar on the same topic, and was invited to speak at the follow-up meeting in 2000.

CRITICAL CARE MEDICINE DEPARTMENT

International Research

In the Critical Care Medicine Department, eight Visiting Fellows performed research in pulmonary disease, HIV, and sepsis. Their home institutions and research areas are as follows:

- Chinese Academy of Medical Sciences, Beijing—(1) mechanisms of nitric oxide control of gene expression and (2) sepsis and lung injury;

- Hunan Medical University, Changsha, China—development of a rapid diagnostic test for *Pneumocystis carinii*;

- Chongqing University, China—evaluation of mutations in genes of *P. carinii* that are targets of drug therapy, to determine whether resistance to therapeutic agents is related to mutations;

- Dailan Medical University, China—responses of epithelial cells to inflammatory mediators and control of arachidonate metabolism in epithelial cells;

- Tongji Medical University, Wuhan, China—nitric oxide synthase signal transduction;

- University of Copenhagen, Denmark—modulation of immune responses to *P. carinii*;

- University of Lotz, Poland—transcriptional regulation of proteins in response to inflammatory mediators in the lung epithelium; and

Hospital General Universitario Gregorio Marañón, Madrid, Spain—mechanisms of cell migration and response in the inflamed lung.

DIAGNOSTIC RADIOLOGY DEPARTMENT

International Research

The Diagnostic Radiology Department hosted the following researchers:

- medical student from the University of Heidelberg, Germany, who was involved in setting up a functional tumor-imaging laboratory during a 3-month rotation in radiology;

- doctoral candidate from Madrid, Spain, at the University of Heidelberg, Germany, for ultrasound research;

- radiologist from Ankara and in the Turkish Army, who served as a Special Volunteer, to analyze spectroscopic imaging and

to help in interpretation of diagnostic studies; and

- medical student from the University of Leicester, England, for a 2-month clinical rotation in neuroradiology.

International Meetings

Staff of the Diagnostic Radiology Department participated at international meetings during FY 00. One staff member was an invited speaker at the 10th Summer Practicum of the Society of Computed Body Tomography and Magnetic Resonance, in Whistler, British Columbia, on August 13–16, 2000. He addressed several subjects—problematic renal masses; hereditary renal disease; MRI of the kidney and adrenal glands; and magnetic resonance angiography (MRA) of the abdomen, including technical advances and functional imaging of tumors. He also conducted a workshop on MRA of small renal masses.

The same staff member was an invited speaker on dynamic enhancement of small renal masses, at a meeting of the European Society of Uroradiology, in London, England, on September 22–26, 2000.

LABORATORY OF DIAGNOSTIC RADIOLOGY RESEARCH

International Meetings

The Chief of the Laboratory of Diagnostic Radiology Research and staff participated at international meetings, in FY 00. The Chief presented a report on a pilot study of recombinant insulin-like growth factor I in multiple sclerosis (MS), at the European Charcot Foundation Symposium on Early Indicators, Early Treatment, and Neuroprotection in MS, in Lausanne, Switzerland, on March 23–25, 2000.

One staff member presented two reports, and another gave a poster presentation, at the conference of the International Society of Magnetic Resonance in Medicine, in Denver, Colorado, on April 1–7, 2000.

HOSPITAL EPIDEMIOLOGY AND QUALITY ASSURANCE SERVICE

International Research

Investigators in the Hospital Epidemiology and Quality Assurance Service continue to collaborate with physicians and nurses at Iwate Medical Hospital, Morioka; Morioka Yuai Hospital; Osaka University Hospital; and St. Marianna Hospital, Sendai, Japan.

The study is designed to accomplish the following purposes:

- evaluate and compare nurses' knowledge of epidemiology, pathogenesis, occupational risks, and appropriate prevention strategies to prevent infection with blood-borne pathogens;

- compare self-reported levels of compliance with recommendations for infection control;

- compare self-reported frequencies of cutaneous exposures to blood; and

- evaluate the effect of educational interventions on nurses' perceived compliance with recommendations and on the frequencies of self-reported exposures to blood.

Phase I of the study is complete. This phase of the research focused on baseline characterization of the nurses' knowledge of epidemiology, pathogenesis, occupational risks, and appropriate prevention strategies in relation to infection with blood-borne pathogens, frequency of exposures, and compliance with infection control procedures. Results were reported at the 4th Decennial Conference on Nosocomial and Healthcare-Associated Infections, in Atlanta, Georgia, on March 5–9, 2000, and at the 38th annual meeting of the Infectious Diseases Society of America, New Orleans, Louisiana, on September 6–9, 2000.

On the basis of the phase I data, an educational intervention was designed and implemented. In July 2000, a cadre of Clinical Center nurses traveled to Japan and trained more than 700 Japanese nurses during a 3-day seminar.

The phase II study, which is under way, consists of a reevaluation of nurses' knowledge and practices after the educational intervention. A survey was administered, and the data will be analyzed soon.

DEPARTMENT OF LABORATORY MEDICINE

International Research

Clinical Chemistry Service

A Senior Staff Fellow from China examined the interference of vitamin C with several common laboratory tests and investigated using aptamers (oligonucleotide ligands) for clinical diagnostic tests.

The collaboration of researchers at the Clinical Center with French and German researchers produced a report on "Human ATP

(adenosine triphosphate)-binding cassette transporter 1 (ABC1): genomic organization and identification of the genetic defect in the original Tangier disease kindred" (*Proceedings of the National Academy of Sciences*, October 1999).

Hematology Service

A French intramural research training award fellow studied murine CD8 responses against bacterially derived protein antigens. These studies may have important implications for design of protein-based vaccines to combat infection and neoplasm.

Immunology Service

A Visiting Associate from the Netherlands worked on (1) characterization of lymphocyte reconstitution after transplantation of nonmyeloablative hematopoietic stem cells, as therapy for chronic granulomatous disease, and (2) characterization of patients with the autoimmune lymphoproliferative syndrome due to Fas mutations. The studies of patients with this syndrome include expression of lymphocyte surface antigens (e.g., alteration of surface glycans), B-cell abnormalities, and B-cell memory (e.g., CD27 expression and somatic mutation of the gene for immunoglobulin).

A Guest Researcher from Turkey evaluated patients for a new defect in the pathway of immune response by type 1 helper T cells (TH1) and worked on an evaluation program for immune disorders.

Microbiology Service

In FY 00, a Fogarty Fellow from Denmark continued his research on *P. carinii*, focusing primarily (1) on development and validation of a diagnostic, real-time, quantitative polymerase chain reaction assay for the organism, with an investigator at the Department of Laboratory Medicine, and (2) on identification and characterization of novel *P. carinii* antigens, with investigators from the Clinical Center's Critical Care Medicine Department and the Division of AIDS (acquired immunodeficiency syndrome), National Institute of Allergies and Infectious Diseases.

NUCLEAR MEDICINE DEPARTMENT

International Research

Four Fogarty Fellows (one from China, one from Japan, and two from Korea) worked in the Monoclonal Antibody Group, Nuclear Medicine Department, on development of radiolabeled variable antibody (Fv) fragments and pretargeted antibody therapy, as diagnostic imaging agents for cancer. This research resulted in four presentations at the 47th Annual Meeting of the Society of Nuclear Medicine, in St. Louis, Missouri, on June 4–8, 2000, and in publication of four articles in peer-reviewed journals: the *Journal of Nuclear Medicine* (February, April, and June 2000) and *Cancer Research* (July 2000).

The Imaging Physics Group, Nuclear Medicine Department, was involved in the following joint efforts:

- collaborative project at INSERM (French National Institutes of Health and Research), Paris, involving investigation of methods to synthesize and combine data on complementary perfusion and function, from gated positron emission tomography (PET) or single photon emission computed tomography scans;

- oral presentation of an abstract on the results of this collaborative project, at the Society of Nuclear Medicine's 47th Annual Meeting, in St. Louis, Missouri, on June 4–8, 2000; and

- collaboration in registration of multimodality images (accurate superposition of images obtained with different techniques in the same subject) by the Imaging Physics Laboratory and the Hospital General Universitario Gregorio Marañón, Madrid, Spain.

International Meetings

A senior member of the Imaging Physics Laboratory gave an invited presentation at the 2nd International Symposium on PET Applications in Oncology, at Universidad Complutense de Madrid Medical School, in Spain, on March 27–30, 2000.

In addition, a Visiting Fellow from Korea in the Imaging Physics Laboratory made an oral presentation at the Society of Nuclear Medicine's 47th Annual Meeting, in St. Louis, Missouri, on June 4–8, 2000.

NURSING DEPARTMENT

International Meetings

Nursing Department staff participated at international meetings in the following capacities:

- gave a poster presentation entitled Gender Differences in Disease Severity, Breathlessness Experience, Quality of Life, and Functional Performance in Persons With Chronic Obstructive Pulmonary Disease, at the European Respiratory Society meeting, in Madrid, Spain, on October 7, 1999;

- gave a poster presentation on The Bereavement Pathway for the Families of Allogeneic Peripheral Blood Stem Cell Transplant Recipients, at the 12th International Symposium: Supportive Care in Cancer, in Washington, D.C., on March 23–25, 2000;

- spoke on (1) The Role of the Advanced Practice Nurse in Transplantation and (2) The Role of the Transplant Coordinator in Education, at the conference of the International Society of Heart and Lung Transplantation, in Osaka, Japan, on April 4–5, 2000;

- made a presentation on The Role of Transplant Coordinators in the United States, at the Transplant Recipient International Organization Conference, in Tokyo, Japan, on April 9, 2000;

- presented the Overview of the Adrenal Gland, at the annual conference of the Endocrine Nurses Society, in Toronto, Ontario, on June 20–24, 2000;

- made poster presentations on (1) Non-myeloablative Allogeneic Peripheral Blood Stem Cell Transplantation: Clinical Overview and Nursing Implications and (2) The Redesigned Role of the Bone Marrow Transplant Coordinator, at the 11th Annual Conference on Cancer Nursing, in Oslo, Norway, on July 31–August 3, 2000; and

- gave presentations on (1) Oncological Advances at the National Institutes of Health, (2) Measures to Ensure Quality in Caring for Oncology Patients, (3) Managing Cancer-Related Fatigue, and (4) Management of Fever/Neutropenia in the Cancer Patient, at the International Conference on Oncology, sponsored by Catholic University of Santiago and held in Santiago, Chile, on September 29–30, 2000.

International Programs and Activities

On April 10–14, 2000, two staff members, together with a representative from the NIH

Office of Loan Repayment and Scholarships and the Deputy Director of the Office of Equal Opportunity and Civil Rights, visited with the deans of the following universities in Puerto Rico to inform them about opportunities in the Nursing Department and to establish working relationships: Metropolitan University, San Juan; Pontifical Catholic University, Ponce; University of Puerto Rico, San Juan and Mayaguez; Turabo University, Gurabo; and Inter-American University, including the Guayama, Metropolitan, and Ponce campuses.

On July 17–18, 2000, representatives from these universities visited the Nursing Department at the Clinical Center and were given a tour of the nearby Children's Inn. They learned about formal educational opportunities in the Nursing Department; the programs of the National Institute of Nursing Research; grant information; bioethics and HIV/AIDS research; the mission of the National Center for Complementary and Alternative Medicine; development of a plan for recruiting Hispanics as subjects in clinical studies; oncology research in children and adults; programs for detection, prevention, and treatment of AIDS; and special features of the nursing recruitment program.

The Nursing Department serves as a host site for the International Oncology Nursing Fellowships sponsored by the International Union Against Cancer, which partners with the Oncology Nursing Society to provide fellowships to nurses from developing countries. When the nurses return to their home institutions, they are expected to create change in the delivery of patient care, based on their experiences at the host site. In FY 00, the Nursing Department received six applications for training and accepted two. However, the International Union Against Cancer funded only one of the applicants, from the Sultanate of Oman.

Four nurses from Ireland spent 1 week in the Nursing Department learning more about oncology nursing, as part of training provided by the consortium among the Department of Health and Children of Ireland, the Department of Health and Social Services for Northern Ireland, and the National Cancer Institute, NIH.

NIH Campus Activities

In FY 00, the Nursing Department hosted two international visitors, providing learn-

ing opportunities in clinical care, research, education, and informatics. Through the Uniformed Services University of the Health Sciences, School of Medicine, Bethesda, Maryland, one physician from the State University of Rio de Janeiro, Brazil, received an overview of the standard clinical desktop and medical information system. Through the University of Maryland, Baltimore, one nurse from National University Hospital, Singapore, participated in a WHO site visit and received an overview of nursing informatics in clinical practice.

In addition, the Nursing Department is frequently consulted through contacts from international conferences, courses, or the Internet, about its standards of practice for nursing and standards of care for patients.

PHARMACY DEPARTMENT

International Research

Pharmacy Department staff participated in several international activities during FY 00, including the following:

- collaboration with investigators in the National Institute of Child Health and Human Development, NIH, to establish sites in Angola and Cape Verde Islands for trials of shigella vaccine;

- formulation and distribution of investigational medications to Argentina, Chile, China, Thailand, the United Kingdom, and Vietnam, as part of ongoing studies with NIH-based investigators; and

- standardization of the chemotherapy procedures for the International Network for Cancer Treatment and Research study of metastatic osteosarcoma in developing countries, including Brazil, China, India, Mexico, the Philippines, and Saudi Arabia.

International Meetings

Staff members in the Pharmacy Department were invited to make presentations at the following international meetings:

- 1st International Workshop on Clinical Pharmacology of HIV Therapy, in Noordwijk, the Netherlands, on March 29–30, 2000;

- International Society of Oncology Pharmacy Practitioners, in Prague, Czech Republic, on April 3–6, 2000;

- joint meeting of the National CIVAS (Centralised Intravenous Addictive Services) Group and the Royal Pharmaceutical Society, in London, England, on July 21, 2000;

- CNN Health Chat on herb–drug interactions, including questions from participants in countries around the world, on July 28, 2000; and

- 40th Interscience Conference on Antimicrobial Agents and Chemotherapy, in Toronto, on September 17–20, 2000.

NIH Campus Activities

International activities of the Pharmacy Department on the NIH campus, in Bethesda, Maryland, included the following:

- Guests from Angola, Czech Republic, Italy, Japan, Slovenia, and Taiwan visited for 1-day programs to learn about pharmacy practice or pharmaceutical research.

- Educational programs on use of medications and compliance with protocols were provided for the Infectious Disease Society of America's HIV Fellowship, to registrants from El Salvador, Malaysia, Nigeria, Tunisia, and Zambia.

- Pharmacy Department staff chaired the Pharmacokinetics–Pharmacodynamics Practice and Research Network (a worldwide network), a focused interest group of the American College of Clinical Pharmacy, for which the world headquarters is located in Kansas City, Missouri.

- A Visiting Fellow from Taiwan spent 3 months in the Pharmacy Department learning skills for the practice of clinical pharmacy.

POSITRON EMISSION TOMOGRAPHY DEPARTMENT

International Research

Members of the Positron Emission Tomography Department continued joint efforts with a major European laboratory, KFA, in Julich, Germany, to develop and analyze muscarinic receptor ligands.

REHABILITATION MEDICINE DEPARTMENT

International Research

The Chief, Biomechanics Section, Rehabilitation Medicine Department, continued to support a collaborative research effort by the National Institute of Neurological Disorders and Stroke, NIH, with the National Research Institute on Aging, Florence, Italy.

In addition, the Biomechanics Laboratory software for motion analysis continued to be licensed through material-transfer agreements to scientists in Australia, Canada, England, Ireland, Italy, and the Netherlands.

International Meetings

Members of the Rehabilitation Medicine Department participated in various capacities in international meetings and research in FY 00. The Chief of the Department presented the keynote address at the founding meeting of the Italian Society for Clinical Movement Analysis, in Rome, on October 28–29, 1999. Also, the Chief was the keynote speaker at an international conference on Cancer Rehabilitation: Integrating Traditional and “Whole-Person” Care, in Montreal, Quebec, on January 21–22, 2000. The speech was entitled The Bridge to Cross Between Organ and Organism. She also spoke on Future Directions in Cancer Rehabilitation.

DEPARTMENT OF TRANSFUSION MEDICINE

International Meetings

The Chief, Department of Transfusion Medicine, served in the following capacities at international meetings in FY 00:

- chaired the 24th International Symposium on Blood Transfusion in Groningen, the Netherlands, on October 4–8, 1999, and spoke on Molecular Biology in Blood Transfusion;

- gave a presentation on granulocyte transfusion at the Transfusion Symposium, at Institutos Medicos Antartida, in Buenos Aires, Argentina, on November 17–20, 1999;

- spoke at the Transfusion Medicine Conference, in Tokyo, Japan, on January 19–23, 2000;

- served on the subcommittee at the National Blood Authority Research Review Committee, in London, England, that discussed the research programs of the Bristol and Cambridge/Collindale Centers and reviewed existing project grants, on February 5–9, 2000; and

- lectured at the 12th World Congress of Anesthesiologists, in Montreal, on June 6–7, 2000.

The Chief, Infectious Diseases Section, served in the following capacities in FY 00:

- by invitation, attended the 2nd International Meeting on Scientific Research Towards the 3rd Millennium, in Cagliari, Italy, on October 7–9, 1999;

- made a presentation at the conference on Managing Hepatitis C at the Turn of the Millennium, in Acapulco, Mexico, on March 23–26, 2000;

- spoke at the 1st International Scientific Symposium on HCV (hepatitis C virus) Antigen, in Paris, France, on March 28–31, 2000;

- by invitation, attended the International Consortium for Blood Safety, in Rust, Austria, and the Annual International Society of Blood Transfusion, in Vienna, during the period July 4–14, 2000; and

- attended and gave a presentation at the meeting on Liver Diseases in the New Millennium, in Shanghai, China, on September 22–27, 2000.

The Chief, Laboratory Services Section, by invitation, worked at the Naval Medical Research Institute, Lima, Peru, to evaluate transient hemolytic anemia, on October 5–12, 1999, and on June 11–16, 2000.

The microbiologist, Infectious Diseases Section, served by invitation in the following capacities:

- speaker at the Institute of Preventative Medicine and at the 10th Regional Conference of the International Society of Blood Transfusion, in Taipei, Taiwan, on November 9–14, 1999;

- speaker at the 2nd International Symposium on Hepatology, in Beijing, China, on December 2–9, 1999; and

- participant in a collaborative study for a molecular epidemiologic survey of transfusion-related viruses, in Kawasaki, Japan, on July 4–23, 2000.

NIH Campus Activities

In FY 00, seven Visiting Fellows (one from Australia, one from China, three from Italy, and two from Japan) and one Special Volunteer funded by the German government worked with staff of the Department of Transfusion Medicine.